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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/665,383

09/16/2003

Juergen Floege

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EXAMINER

HUYNH, PHUONG N

ART UNIT

PAPER NUMBER

1644

MAIL DATE

DELIVERY MODE

05/21/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/665,383

Applicant(s)

FLOEGE ET AL.

Examiner

Phuong Huynh

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1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 February 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,6,7,22-28 and 31-33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 6-7, 22-28 and 31-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 September 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/21/07 has been entered.
2. Claims 1-3, 6-7, 22-28 and 31-33 are pending and are being acted upon in this Office Action.
3. The following are new ground of rejection.
4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
5. Claims 1-3, 6-7, 22-28 and 31-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for a method of effectively ameliorating nephritis, comprising selecting an animal in need of treatment for nephritis, and administering to said animal a therapeutically effective dose of a neutralizing antibody, or binding fragment thereof that binds to platelet derived growth factor-DD (PDGF-DD), wherein said neutralizing antibody, or binding fragment thereof, neutralizes PDGF-DD-induced mitogenic activity of mesangial cells, and wherein said neutralizing antibody, or binding fragment thereof, comprises fully human anti-PDGF-DD monoclonal antibody having the variable region (CDRs1-3) of the heavy chain consisting of the amino acid sequence of SEQ ID NO:2 and the variable region (CDRs1-3) of the light chain consisting of the amino acid sequence of SEQ ID NO:4, or a fully human antibody having the variable region (CDRs1-3) of the heavy chain consisting of the amino acid sequence of SEQ ID NO:22 and the variable region (CDRs1-3) of the light chain consisting of the amino acid sequence of SEQ ID NO:24, or a fully human antibody having the variable region (CDRs1-3) of the heavy chain consisting of the amino acid sequence of SEQ ID NO:38 and the variable region (CDRs1-3) of the light chain consisting of the amino acid sequence of SEQ ID NO:40 and wherein said nephritis is selected from the group consisting of mesangial proliferative nephritis,

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mesangial proliferative glomerulonephritis, and glomerular nephritis, **does not** reasonably provide enablement for a method of effectively treating nephritis that encompasses preventing nephritis as set forth in claims 1-3, 6-7, 22-28 and 31-33. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

Claims 1-3, 6-7, 22-28 and 31-33 are drawn to a method of *preventing* nephritis such as mesangial proliferative nephritis, mesangial proliferative glomerulonephritis, or glomerular nephritis by administering to the animal in need thereof a neutralizing antibody or binding fragment thereof wherein the monoclonal antibody having *any* variable region of the heavy chain of SEQ ID NO: 2 and *any* variable region of the light chain of SEQ ID NO: 4 or an antibody in the same antigen-binding bin as fully human anti-PDGF-DD antibody having *any* variable region of the heavy chain consisting of the amino acid sequence of SEQ ID NO:2 and *any* variable region of the light chain consisting of the amino acid sequence of SEQ ID NO:4, wherein said antibody in the same antigen-binding bin is selected from a fully human antibody having *any* variable region of the heavy chain consisting of the amino acid sequence of SEQ ID NO:22 and *any* variable region of the light chain consisting of the amino acid sequence of SEQ ID NO:24, or a fully human antibody having *any* variable region of the heavy chain consisting of the amino acid sequence of SEQ ID NO:38 and *any* variable region of the light chain consisting of the amino acid sequence of SEQ ID NO:40. The antibody administered to the animal is any variable region of the recited SEQ ID NOs: and not the antibody comprising the variable region comprising all six variable domains of immunoglobulin heavy and light chains.

Enablement is not commensurate in scope with methods of effectively *preventing* nephritis such as mesangial proliferative nephritis, mesangial proliferative glomerulonephritis and glomerular nephritis, such treating include those in who the disorder is to be prevented by

administering to said animal a therapeutically effective dose of any neutralizing antibody, or binding fragment thereof, that binds to platelet derived growth factor-DD (PDGF-DD) mentioned above.

The specification at page 26 paragraph [0079] defines the term "Treatment" refers to both therapeutic treatment and *prophylactic* or preventative measures, wherein the object is to *prevent* or slow down (lessen) the targeted pathologic condition or disorder. Those in need of treatment include those already with the disorder as well as those prone to have the disorder or *those in whom the disorder is to be prevented*". The specification discloses administering a fully human anti-PDGF-DD monoclonal antibody mAb 6.4 comprising immunoglobulin heavy chain comprising the amino acid sequence of SEQ ID NO: 2 and immunoglobulin light chain comprising the amino acid sequence of SEQ ID NO: 4 to nephritic male Wistar rats that have been induced with anti-Thy-1.1 (an acute rat model of mesangial proliferative glomerulonephritis). The treatment reduces glomerular proliferation as measured by BrdU incorporation, reduces mesangial cells proliferation, see pages 73-80, page 58. The anti-PDGF-DD antibody was administered on day 3 and on day 5 after disease induction, see page 73, paragraph [0226].

The specification does not teach a method of preventing nephritis in any animal by administering any neutralizing antibodies mentioned above. The specification fails to provide any guidance and *in vivo* working example as how to identify an individual such as a human who is prone to have any nephritis, any nephritis such as mesangial proliferative nephritis, mesangial proliferative glomerulonephritis, and glomerular nephritis or those in whom the disorder could be prevented.

Ahmad et al (Nephron 84(4): 342-6, April 2000; PTO 892) teach progression of disease involving mesangial IgM nephropathy or focal segmental glomerulosclerosis is often unpredictable from its clinical presentation in children, see abstract, in particular.

Further, there is insufficient guidance as to the effective dose and *in vivo* working example demonstrating the claimed method *could prevent* any chronic nephritis in any animal, any animal such as humans by administering any one of the fully human antibodies as recited in the claims.

Ostendorf et al (J Am Soc Nephrol 17: 1054-1062, 2006; PTO 892) teach anti-thy-1 model is a reversible non-progressive rat model of mesangial cell proliferation and matrix accumulation (see page 1054, col. 2, in particular). Administering fully human PDGF-D

monoclonal antibody such as CR002 acutely reduces mesangial cell proliferation, glomerular influx of monocytes and/macrophages in anti-thy1 induced rat model, see page 1060, col. 2, in particular). Inhibition of PDGF-D during the acute phase of anti-thy1.1 induced nephritis markedly reduces both glomerular tubulointerstitial scarring on day 56 after disease induction. However, albuminuria was not reduced during the course of the disease in the anti-PDGF-D treated group, see page 1060, col. 2, in particular). Given that renal diseases in humans are progressive in nature and eventually result in end-stage renal disease, especially chronic glomerulonephritis, and mesangial proliferative glomerulonephritis, it is not clear the reliance of this acute reversible non-progressive rat model of mesangial cell proliferation is sufficient to generalize to chronic glomerulonephritis in human.

Further, the claims encompass any combination of heavy and light chain CDR1, CDR2, and CDR3 from immunoglobulin heavy and light chains. There is insufficient guidance as to which combination of CDR, CDR2, and/or CDR3 from immunoglobulin heavy and light chains would maintain the same binding specificity as the claimed antibody that binds specifically to human PDGF-DD for the claimed method. The term "variable region" or "a variable region" could be any CDRs or any fragment of any CDRs of the variable region from the heavy and light chains of SEQ ID NO: 2 and SEQ ID NO: 4, respectively. Likewise, a variable region of heavy chain SEQ ID NO: 22 and a variable region of light chain of SEQ ID NO: 24 could be any combination of CDR1, CDR2, CDR3 from said heavy and light chains.

However, the binding specificity of an antibody molecule is dependent on its three dimensional structure, which in turn is dependent on its primary amino acid sequence of all three variable domains (CDRs1-3) from immunoglobulin heavy chain and all three CDRs 1-3 from immunoglobulin light chain. Changing the amino acid sequence of an antibody may adversely affect its binding activity. Likewise, fragments of the antibody may not retain the appropriate three dimensional structure necessary to foster binding activity.

Rudikoff *et al* (Proc Natl Acad Sci USA 79: 1979, 1982; PTO 892) teach even a single amino acid substitution from glutamic acid to alanine at position 35 in the first hypervariable or complementarity-determining region (one of the CDR) of an antibody resulted altered binding specificity of the antibody (See abstract, in particular).

There are also critical framework residues which are important in positioning the CDRs for interaction with antigen or which are involved in interactions between the heavy and light chains.

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Landolfi et al (J Immunology 166: 1748-1754, 2001; PTO 892) teach amino acid substitutions at the framework position 11 to from Leu (L) to Val (V) and V_H position 38 from lys (K) to Arg (R) mutation resulted in loss of antibody neutralizing activity (see entire document, page 1751, col. 2, in particular). Landolfi et al teach further teach changing CH1 residue 148 diminished the ability of the antibody to neutralize IFN- γ (see abstract, in particular).

Therefore, it is not clear that any combination of any variable region (CDR regions) or fragments from hypervariable regions from heavy and light chains will have the asserted utility of binding to human PDGF-D, without further guidance from the specification. Further, there is insufficient working example demonstrating any combination of CDR regions will have the asserted binding specificity to all PDGF-D, in turn, would be useful for any purpose. The same reasoning applies to the other antibodies in the same antigen-binding bin as fully human anti-PDGF-DD antibody.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

6. Claims 1-3, 6-7, 22-28 and 31-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-3, 6-7, 22-28 and 31-33 are drawn to a method of *preventing* nephritis such as mesangial proliferative nephritis, mesangial proliferative glomerulonephritis, or glomerular nephritis by administering to the animal in need thereof a neutralizing antibody or binding fragment thereof wherein the monoclonal antibody having *any* variable region of the heavy chain of SEQ ID NO: 2 and *any* variable region of the light chain of SEQ ID NO: 4 or an antibody in

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the same antigen-binding bin as fully human anti-PDGF-DD antibody having *any* variable region of the heavy chain consisting of the amino acid sequence of SEQ ID NO:2 and *any* variable region of the light chain consisting of the amino acid sequence of SEQ ID NO:4, wherein said antibody in the same antigen-binding bin is selected from a fully human antibody having *any* variable region of the heavy chain consisting of the amino acid sequence of SEQ ID NO:22 and *any* variable region of the light chain consisting of the amino acid sequence of SEQ ID NO:24, or a fully human antibody having *any* variable region of the heavy chain consisting of the amino acid sequence of SEQ ID NO:38 and *any* variable region of the light chain consisting of the amino acid sequence of SEQ ID NO:40. The antibody or binding fragment thereof to be administered to the animal encompasses any variable region of the recited SEQ ID NOs: and not the antibody comprising the variable region comprising all six variable domains (CDRs 1-3) of immunoglobulin heavy and light chains.

The specification does not reasonably provide a **written description** of the structure of antibody or binding fragment thereof that binds to PDGF-DD such as which combination of CDR, CDR2, and/or CDR3 of “a variable region” or “variable region” from immunoglobulin heavy and light chains would maintain the same binding specificity as the claimed antibody that binds specifically to human PDGF-DD for the claimed method for the claimed method of effectively treating nephritis that encompasses preventing nephritis as set forth in claims 1-3, 6-7, 22-28 and 31-33.

The term “variable region” or “a variable region” could be any CDRs or any fragment of any CDRs of the variable region from the heavy and light chains of SEQ ID NO: 2 and SEQ ID NO: 4, respectively. Likewise, a variable region of heavy chain SEQ ID NO: 22 and a variable region of light chain of SEQ ID NO: 24 could be any combination of CDR1, CDR2, CDR3 from said heavy and light chains.

The specification at page 26 paragraph [0079] defines the term “Treatment” refers to both therapeutic treatment and *prophylactic* or preventative measures, wherein the object is to *prevent* or slow down (lessen) the targeted pathologic condition or disorder. Those in need of treatment include those already with the disorder as well as those prone to have the disorder or *those in whom the disorder is to be prevented*”. The specification discloses administering a fully human anti-PDGF-DD monoclonal antibody mAb 6.4 comprising immunoglobulin heavy chain comprising the amino acid sequence of SEQ ID NO: 2 and immunoglobulin light chain comprising the amino acid sequence of SEQ ID NO: 4 to nephritic male Wistar rats that have

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been induced with anti-Thy-1.1 (an acute rat model of mesangial proliferative glomerulonephritis). The treatment reduces glomerular proliferation as measured by BrdU incorporation, reduces mesangial cells proliferation, see pages 73-80, page 58. The anti-PDGF-DD antibody was administered on day 3 and on day 5 after disease induction, see page 73, paragraph [0226].

There is inadequate disclosure as to which combination of CDR, CDR2, and/or CDR3 from immunoglobulin heavy and light chains would maintain the same binding specificity as the claimed antibody that binds specifically to human PDGF-DD for the claimed method. The term "variable region" or "a variable region" could be any CDRs or any fragment of any CDRs of the variable region from the heavy and light chains of SEQ ID NO: 2 and SEQ ID NO: 4, respectively. Likewise, a variable region of heavy chain SEQ ID NO: 22 and a variable region of light chain of SEQ ID NO: 24 could be any combination of CDR1, CDR2, CDR3 from said heavy and light chains.

However, the binding specificity of an antibody molecule is dependent on its three dimensional structure, which in turn is dependent on its primary amino acid sequence of all three variable domains (CDRs1-3) from immunoglobulin heavy chain and all three CDRs 1-3 from immunoglobulin light chain. Changing the amino acid sequence of an antibody may adversely affect its binding activity. Likewise, fragments of the antibody may not retain the appropriate three-dimensional structure necessary to foster binding activity.

Rudikoff *et al* (Proc Natl Acad Sci USA 79: 1979, 1982; PTO 892) teach even a single amino acid substitution from glutamic acid to alanine at position 35 in the first hypervariable or complementarity-determining region (one of the CDR) of an antibody resulted altered binding specificity of the antibody (See abstract, in particular).

There are also critical framework residues which are important in positioning the CDRs for interaction with antigen or which are involved in interactions between the heavy and light chains.

Landolfi *et al* (J Immunology 166: 1748-1754, 2001; PTO 892) teach amino acid substitutions at the framework position 11 to from Leu (L) to Val (V) and V_H position 38 from Lys (K) to Arg (R) mutation resulted in loss of antibody neutralizing activity (see entire document, page 1751, col. 2, in particular). Landolfi *et al* teach further teach changing CH1 residue 148 diminished the ability of the antibody to neutralize IFN- γ (see abstract, in particular).

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Therefore, the antibody or binding fragment thereof comprising any combination of any variable region (CDR regions) or fragments from hypervariable regions from heavy and light chains that to human PDGF-D for the claimed method of treating nephritis is not adequately described, much less for preventing any nephritis in humans.

With the exception of the specific a method of effectively ameliorating nephritis, comprising selecting an animal in need of treatment for nephritis, and administering to said animal a therapeutically effective dose of a neutralizing antibody, or binding fragment thereof that binds to platelet derived growth factor-DD (PDGF-DD), wherein said neutralizing antibody, or binding fragment thereof, neutralizes PDGF-DD-induced mitogenic activity of mesangial cells, and wherein said neutralizing antibody, or binding fragment thereof, comprises fully human anti-PDGF-DD monoclonal antibody having the variable region (CDRs1-3) of the heavy chain consisting of the amino acid sequence of SEQ ID NO:2 and the variable region (CDRs1-3) of the light chain consisting of the amino acid sequence of SEQ ID NO:4, or a fully human antibody having the variable region (CDRs1-3) of the heavy chain consisting of the amino acid sequence of SEQ ID NO:22 and the variable region (CDRs1-3) of the light chain consisting of the amino acid sequence of SEQ ID NO:24, or a fully human antibody having the variable region (CDRs1-3) of the heavy chain consisting of the amino acid sequence of SEQ ID NO:38 and the variable region (CDRs1-3) of the light chain consisting of the amino acid sequence of SEQ ID NO:40 and wherein said nephritis is selected from the group consisting of mesangial proliferative nephritis, mesangial proliferative glomerulonephritis, and glomerular nephritis, there is a lack of any data to support the claimed method of *preventing* nephritis such as mesangial proliferative nephritis, mesangial proliferative glomerulonephritis, and glomerular nephritis in any animal, any animal such as humans.

One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species of antibody or binding fragment thereof to describe the genus for the claimed method of treating nephritis the encompasses preventing nephritis in those who prone to have nephritis or those in whom the disorder is to be prevented. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co.* 43 USPQ2d 1398; *University of Rochester v. G.D. Searle & Co.*, 69 USPQ2d 1886 (CA FC2004).

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

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7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-3, 22-28 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 7,135,174 B2 (filed Jan 7, 2002; PTO 892) in view of Johnson et al (of record, J Exp Med 175: 1413-1416, May 1992; PTO 892).

The '174 patent teaches various fully human anti-PDGF-DD neutralizing monoclonal antibodies having variable region of the heavy chain consisting of the amino acid sequence of SEQ ID NO: 48 which is 100% identical to the claimed SEQ ID NO: 2 (see reference SEQ ID NO: 48, col. 25, lines 5-67, col. 32, lines 17-33, col. 28, in particular) and a variable region of the light chain consisting of the amino acid sequence of SEQ ID NO: 49, which is 100% identical to the claimed SEQ ID NO: 4 (see reference SEQ ID NO: 49, in particular) or binding fragment thereof such as Fv, F(ab')₂, Fab (see col. 28, lines 30-37, in particular). The '174 patent teaches another fully human anti-PDGF-DD monoclonal antibody having variable region of the heavy chain consisting of the amino acid sequence of SEQ ID NO: 21 which is 100% identical to the claimed SEQ ID NO: 22 (see reference SEQ ID NO: 21, col. 25, lines 5-47, in particular) and a variable region of the light chain consisting of the amino acid sequence of SEQ ID NO: 22, which is 100% identical to the claimed SEQ ID NO: 24 (see reference SEQ ID NO: 22, in particular). The '174 patent teaches another fully human anti-PDGF-DD monoclonal antibody having variable region of the heavy chain consisting of the amino acid sequence of SEQ ID NO: 29 which is 100% identical to the claimed SEQ ID NO: 38 (see reference SEQ ID NO: 29, col. 25,

lines 5-47, in particular) and a variable region of the light chain consisting of the amino acid sequence of SEQ ID NO: 30, which is 100% identical to the claimed SEQ ID NO: 40 (see reference SEQ ID NO: 22, in particular). The reference antibodies are fully human IgG2 heavy chain (see col. 47-48, in particular). The reference neutralizing antibody comprises a fully human IgG2 heavy chain and a human kappa light chain and a human heavy chain, see col. 26, lines 1-2, in particular). The reference monoclonal antibodies has a Kd in the range of about 10^{-6} to 10^{-11} M as measured in either solid phase or solution phase (see col. 32, lines 34-42, in particular). The '174 patent further teaches the reference antibodies are useful for treating human diseases such as inflammation (see col. 25, lines 42-47, in particular) or proliferation or growth of fibroblast or matrix invasion (see col. 33, lines 10-16, col. 14, lines 12, in particular). The fully human antibodies can be expected to provide a substantial advantage in the treatment of chronic and recurring human diseases, such as inflammation, autoimmunity, and cancer, which require repeated antibody administrations (see col. 25, lines 42-47, in particular). The reference antibodies obviously bind to PDGF-D dimer (PDGF-DD) given the reference antibodies have the same heavy and light chains as the claimed antibodies.

The invention differs from the teachings of the reference only in that method of treating nephritis wherein the nephritis is mesangial proliferative nephritis instead of any inflammation, autoimmunity or cancer.

Johnson et al teach a method of treating nephritis by neutralizes PDGF-induced mitogenic activity by administering to an animal such as rat that was induced with anti-Thy-1 antibody (a model for mesangial proliferative nephritis or glomerulonephritis) a neutralizing antibody such as anti-PDGF antibody (see entire document, col. 1, abstract, page 1414, col. 2, last paragraph, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to treat mesangial proliferative nephritis as taught by Johnson et al by substituting the antibody that binds to PDGF-B in a method of treating nephritis such as mesangial proliferative nephritis as taught by the Johnson et al for the fully human anti-PDGF-DD neutralizing monoclonal antibodies that is useful for human diseases such as inflammation (see col. 25, lines 42-47, in particular) or proliferation or growth of fibroblast or matrix invasion (see col. 33, lines 10-16, col. 14, lines 12, in particular) as taught by the '174 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

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One having ordinary skill in the art would have been motivated to do this because fully human antibodies can be expected to provide a substantial advantage in the treatment of chronic and recurring human diseases, such as inflammation, autoimmunity, and cancer, which require repeated antibody administrations as taught by the '174 patent (see col. 25, lines 42-47, in particular). Johnson et al teach administering neutralizes PDGF antibody is useful in treating PDGF-induced mitogenic activity in an animal that has been identified with mesangial proliferative nephritis or glomerulonephritis, see entire document, abstract, in particular).

10. Claims 6-7 and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 7,135,174 B2 (filed Jan 7, 2002; PTO 892) in view of Johnson et al (of record, J Exp Med 175: 1413-1416, May 1992; PTO 892) as applied to claims 1-3, 22-28 and 33 mentioned above and further in view of US Pat No. 6,706,687 (filed Nov 10, 1999; PTO 892).

The combined teachings of the '174 patent and Johnson et al have been discussed supra.

The invention in claims 6 and 31 differs from the teachings of the reference only in that the method of treating nephritis wherein the administration is via subcutaneous injection.

The invention in claims 7 and 32 differs from the teachings of the reference only in that the method of treating nephritis wherein the administration is via intramuscular injection.

The '687 patent teaches administering PDGF-D antagonist such as antibody that binds to PDGF-DD (PDGF dimer) via suitable route such as subcutaneous or intramuscular injection (see col. 13, lines 3-10, in particular) to treat PDGF-D related diseases such as kidneys (see col. 11, lines 54 bridging col. 12, lines 1-6, in particular) of PDGF-D induced proliferation (see col. 24, lines 46, in particular). The '687 patent teaches the route of administration is known to one skilled in the art such as attending physician or veterinarian (see col. 13, lines 3-7, in particular).

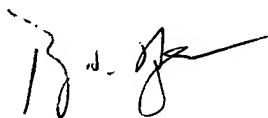
Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer the fully human anti-PDGF-DD neutralizing monoclonal antibodies that is useful for human diseases as taught by the '174 patent via a suitable route such as subcutaneous or intramuscular injection as taught by the '687 patent for a method of treating nephritis as taught by Johnson et al. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the route of administration is known to one skilled in the art such as the attending physician or

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veterinarian as taught by the '687 patent (see col. 13, lines 3-7, in particular) and it is also routine within the purview of one skilled in the art. Fully human antibodies can be expected to provide a substantial advantage in the treatment of chronic and recurring human diseases, such as inflammation, autoimmunity, and cancer, which require repeated antibody administrations as taught by the '174 patent (see col. 25, lines 42-47, in particular). Johnson et al teach administering neutralizes PDGF antibody is useful in treating PDGF-induced mitogenic activity in an animal that has been identified with mesangial proliferative nephritis or glomerulonephritis, see entire document, abstract, in particular).

11. No claim is allowed.
12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Thursday from 9:00 a.m. to 6:30 p.m. and alternate Friday from 9:00 a.m. to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.
13. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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